UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,397		Shizuo Akira	49862	1566

7590 07/30/2002

DIKE, BRONSTEIN, ROBERTS & CUSHMAN
INTELLECTUAL PROPERTY PRACTICE GROUP
P.O. BOX 9169
EDWARDS, & ANGELL
Boston, MA 02209

EXAMINER
PROUTY, REBECCA E

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/30/2002 12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/582,397	Akira et al.
Examiner	**Art Unit**
Rebecca Prouty	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 18, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above, claim(s) *4 and 5* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3 and 6-8* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Jan 16, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *1*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicant's election without traverse of Group I, Claims 1-3 and 6-8 in Paper No. 11 is acknowledged.

Claims 4 and 5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 11.

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the specification. It is particularly noted that Figures 3 and 4 show sequences for which the corresponding SEQ ID NO is not shown either in the figure itself nor in the corresponding Brief description thereof. See particularly 37 CFR 1.821(d).

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-3 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter. In the absence of the hand of man, naturally occurring proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). This rejection may be overcome

by amending the claims to contain wording such as "An isolated and purified protein ..." .

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 8 are indefinite in the recitation of "which acts on the immune response mechanism" and "which is a preventive or therapeutic agent for diseases involving the I-TRAF or the TRAF molecule" as it is unclear how these statements limit the compositions of Claim 6 (from which they depend).

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to a genus of proteins capable of activating transcription factor NF-κB. The specification teaches the structure of only a two representative species of such proteins, i.e., SEQ ID NOS:2 and 4. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of activating transcription factor NF-κB. Given

this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for proteins comprising SEQ ID NO:2 or SEQ ID NO:4 and pharmaceutical compositions thereof, does not reasonably provide enablement for any protein capable of activating transcription factor NF-κB. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1-3 and 6-8 are so broad as to encompass any protein capable of activating transcription factor NF-κB. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of

modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of SEQ ID NOS:2 and SEQ ID NO:4.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any protein capable of activating transcription factor NF-κB because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting NF-κB activating activity; (B) the general tolerance of IKK kinases to modification and extent of

such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of the proteins of SEQ ID NOS:2 or 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of proteins having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country,

> more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by Shimada et al.

Shimada et al. teach the cloning and expression of IKK-i having a sequence identical to SEQ ID NO:2

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagase et al. (EMBL entry D63485) as evidenced by Cao (US Patent 5,776,717).

Nagase et al. teach a human gene (KIAA0151) and encoded protein identical to the protein of SEQ ID NO:2. Cao evidence that the translation product of the human KIAA0151 gene is an IκB kinase and binds and phosphorylates TRAF (see particularly column 6, lines 59-67).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly

owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimada et al. in view of Mercurio et al.

Shimada et al. is discussed above. They do not specifically disclose pharmaceutical compositions of the IKK kinase.

Mercurio et al. teach that IKK kinases activate transcription of NF-κB regulated genes which regulates the critical pathways of inflammation, proliferation and apotosis and thus drugs which modulate the activation and function of these kinases are likely to have therapeutic value in treatment of inflammatory, neurodegenerative diseases and cancer.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the protein of Shimada et al. with an acceptable carrier in order to use it to treat such conditions.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nagase et al. in view of Cao and Mercurio et al.

Nagase et al. and Cao are discussed above. They do not specifically disclose pharmaceutical compositions of the IKK kinase.

Mercurio et al. teach that IKK kinases activate transcription of NF-κB regulated genes which regulates the

critical pathways of inflammation, proliferation and apotosis and thus drugs which modulate the activation and function of these kinases are likely to have therapeutic value in treatment of inflammatory, neurodegenerative diseases and cancer.

Therefore, it would have been obvious to one of ordinary skill in the art to combine the protein of Nagase et al. which is shown by Cao to be an IKK kinase with an acceptable carrier in order to use it to treat such conditions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca Prouty, Ph.D. whose telephone number is (703) 308-4000. The examiner can normally be reached on Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rebecca Prouty
Primary Examiner
Art Unit 1652